



TITLE:

## <Division of Synthetic Chemistry> Synthetic Organic Chemistry

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# Division of Synthetic Chemistry - Synthetic Organic Chemistry -

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Prof. ZIPSE, Hendrik

University of Dehli, India, 25 March 2005  
Ludwig-Maximilians-Universität in München, Germany, 16 September 2005

## Scope of Research

The research interests of the laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the areas of asymmetric alkylation of carbonyl compounds based on “memory of chirality”, nucleophilic catalysis for fine organic synthesis, synthesis of unusual amino acids and nitrogen heterocycles, visualization of molecular information by functionalized phenolphthaleins, use of homooxalixarene for molecular recognition, and the structural and functional investigation of homo- and heterochiral oligomers.

## Research Activities (Year 2005)

### Presentations

Design and Development of the Asymmetric Reactions Based on Memory of Chirality, Kawabata T, 125th Annual Meeting of the Pharmaceutical Society of Japan, 29 March.

Enantioselective Acceleration in Asymmetric Acylation of Alcohols Promoted by Chiral Nucleophilic Catalysts, Kawabata T, Molecular Chirality 2005, 7 June.

Temperature-Dependent Coloration of Phenolphthalein Derivatives with Alkali Metals, Tanima D, 35th Symposium on Structural Organic Chemistry, 9 September.

Memory of Chirality at Room Temperature, Monguchi D, 31st Symposium on Progress in Organic Reactions and Syntheses, 7 November.

Stereochemical Reversal in Asymmetric Cyclization via Memory of Chirality, Kawabata T, Pacificchem 2005, 15 December.

### Grants

Kawabata T, Advanced Molecular Transformation with Functional Carbanions, Grant-in Aid for Scientific Research on Priority Areas, 1 October 2005 - 31 March 2009.

Tsubaki K, Synthesis and Properties of Optically Active Oligonaphthalene Derivatives, Grant-in-Aid for Exploratory Research, 1 April 2005 - 31 March 2007.

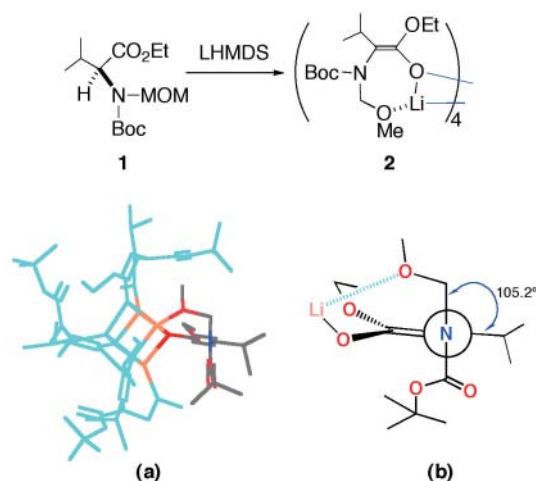
Kawabata T, Synthesis of Highly Functionalized Heterocycles by Asymmetric Cyclization via Memory of Chirality, Grant-in-Aid for Scientific Research, 30 September 2005 - 29 September 2007.

Kawabata T, Development of  $C_2$ -Symmetric Chiral Nucleophilic Catalysts and their Use in Asymmetric C-C Bond Formation, Grant-in-Aid for Scientific Research, 25 June 2004 - 24 June 2006.

Kawabata T, Design of a New Generation of Nucleophilic Catalysts and Selective Reactions, Grant-in-Aid for

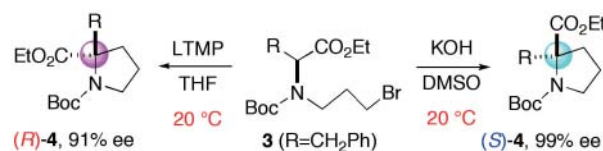
## An X-Ray Structure of an Axially Chiral Enolate

An X-ray crystal structural analysis of an axially chiral enolate has been performed for the first time. A single crystal of a lithium enolate formed by treatment of valine derivative **1** with lithium hexamethyldisilazide (LHMDS) in a mixture of pentane and *t*-butyl methyl ether at 0°C. The tetrameric Li enolate has a cubic core consisting of four Li and four O atoms surrounded by four enolate sub-units (Figure 1, a). Configuration of the tetrameric enolate is (a*S*,a*S*,a*R*,a*R*), which is the result of racemization of chiral C-N axes due to high temperature (0°C) employed for the enolate formation. The nitrogen atom of the enolate is almost completely planar (Figure 1, b). A plane consisting of the planar nitrogen and the substituents forms an angle of 105.2° with that of an enolate plane. This clearly indicates axial chirality of the enolate structure in a solid state. We had already proposed, based on kinetic data, an axially chiral nonracemic enolate intermediate as a crucial intermediate for the asymmetric induction via memory of chirality. This crystal structure is the first concrete evidence for an axially chiral enolate.



**Figure 1.** (a) X-ray structure of **2**. An enolate unit of the tetrameric enolate is colored. Three Li atoms directly connected to an oxygen atom of the colored enolate unit are colored orange. (b) Schematic view of an enolate unit, indicating axial chirality.

## Stereochemical Reversal in Asymmetric Cyclization: Enolate Chemistry at Room Temperature



Treatment of an amino acid derivative **3** by potassium hexamethyldisilazide (KHMDs) in DMF at -60°C gave (*S*)-**4** in 98% ee, while that by KOH in DMSO at room temperature gave (*S*)-**4** even in higher enantioselectivity (99% ee). This could be ascribed to the enhanced reactivity of an amine-free potassium enolate generated by KOH in DMSO. Contrary to this process, treatment of **3** with lithium 2,2,6,6-tetramethylpiperidide (LTMP) in THF at room temperature gave (*R*)-**4** in inversion of the configuration in 91% ee. Interestingly, the similar treatment of **3** with LTMP at -60°C gave (*R*)-**4** in much lower enantioselectivity (41% ee).

## Optical Properties of Oligo(2,3-dioxyfunctionalized)naphthalenes

A series of oligo(2,3-dioxyfunctionalized)naphthalenes **5-7** that possess two pyrene groups on the central scaffolding oxygen functions are synthesized. When the naphthalene units are selectively excited at 310 nm, the fluorescence from the pyrene units was observed. This result demonstrates that an effective intramolecular energy transfer occurs from the naphthalene units to the pyrene units. The intramolecular energy transfer quantum yields of **5-7** were around 20% regardless of the number of naphthalene units. Thus, the optical properties of oligonaphthalenes are more than sum of the discrete naphthalene units. These properties are expected to be produced by coupling the transition moments that run parallel to the minor axis of the naphthalene ring.



Scientific Research (B) (2), 1 April 2002 - 31 March 2005.

### Awards

Tanima D, Best Poster Award, 11th Summer Meeting of Functional Host-Guest Chemistry (Toyama), 28 July 2005.

Monguchi D, Best Poster Award, 25th Seminar on Syn-

thetic Organic Chemistry for Young Scientists, 24 November 2005.

Takaishi K, Best Poster Award, 25th Seminar on Synthetic Organic Chemistry for Young Scientists, 24 November 2005.